



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: DePAOLI, Alex M. *et al.*

APPLICATION No.: 10/623,189

FILED: July 18, 2003

FOR: USE OF LEPTIN FOR TREATING HUMAN  
LIPOATROPHY AND METHODS OF DETERMINING  
PREDISPOSITION TO SAID TREATMENT

EXAMINER:

ART UNIT:

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is being deposited on November 12, 2003, with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

*Deborah Muench*  
DEBORAH MUENCH

**INFORMATION DISCLOSURE STATEMENT WITHIN THREE MONTHS OF  
APPLICATION FILING OR BEFORE FIRST ACTION – 37 C.F.R. § 1.97(b)**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

**1. Timing of Submission**

This information disclosure is being filed within three months of the filing date of this application or date of entry into the national stage of an international application or before the mailing date of a first Office action on the merits, whichever occurs last [37 C.F.R. § 1.97(b)]. The references listed on the enclosed Form PTO-1449 (modified) may be material to the examination of this application; the Examiner is requested to make them of record in the application.

**2. Cited Information**

☒ Copies of the following references are enclosed:

- ☐ All cited references
- ☐ References marked by asterisks
- ☒ The following: B1-B33 and C1-C44

☐ Copies of the following references can be found in parent U.S. Application No. \_\_\_\_\_:

- ☐ All cited references
- ☐ References marked by asterisks
- ☐ The following:

- ☒ This application was filed after 30 June 2003 and no copies of U.S. patents nor published applications are enclosed (See Notice of Deputy Commissioner Kunin on 11 July 2003).
- ☐ The following references are not in English. For each such reference, the undersigned has enclosed (i) a translation of the reference; (ii) a copy of a communication from a foreign patent office or International Searching Authority citing the reference, (iii) a copy of a reference which appears to be an English-language counterpart, or (iv) an English-language abstract for the reference prepared by a third party. Applicant has not verified that the translation, English-language counterpart or third-party abstract is an accurate representation of the teachings of the non-English reference, though, and reserves the right to demonstrate otherwise.
- ☐ All cited references  
☐ References marked by ampersands  
☐ The following:

**3. Effect of Information Disclosure Statement (37 C.F.R. § 1.97(h))**

This Information Disclosure Statement is not to be construed as a representation that: (i) a search has been made; (ii) additional information material to the examination of this application does not exist; (iii) the information, protocols, results and the like reported by third parties are accurate or enabling; or (iv) the cited information is, or is considered to be, material to patentability. In addition, applicant does not admit that any enclosed item of information constitutes prior art to the subject invention and specifically reserves the right to demonstrate that any such reference is not prior art.

**4. Fee Payment**

No fees are believed due because this Information Disclosure Statement is being filed before the mailing date of the first Office Action.

- ☐ Applicant further submits that no fee is due in light of the following certification under 37 C.F.R. § 1.97(e) (check only one):
- ☐ In accordance with 37 C.F.R. § 1.97(e)(1), the undersigned hereby states that each item of information submitted herewith was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement; or
- ☐ In accordance with 37 C.F.R. § 1.97(e)(2), the undersigned hereby states that no item of information submitted herewith was cited in a communication from a foreign patent office in a counterpart foreign application, or, to the knowledge of the person signing the

certification after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c), more than three months prior to the filing of this statement.

However, should the Commissioner determine that fees are due in order for this Information Disclosure Statement to be considered, the Commissioner is hereby authorized to charge such fees to Deposit Account No. **50-2586**.

**5. Patent Term Adjustment (37 C.F.R. § 1.704(d))**

- ☐ The undersigned states that each item of information submitted herewith was cited in a communication from a foreign patent office in a counterpart application and that this communication was not received by any individual designated in 37 C.F.R. § 1.56(c) more than thirty days prior to the filing of this statement. 37 C.F.R. § 1.704(d).

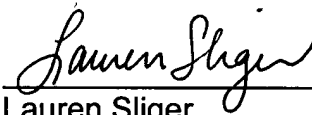
**PAYMENT AND/OR AUTHORIZATION TO CHARGE FEES:**

- ☐ A check in the amount of \_\_\_\_\_ is enclosed for the above fee(s).
- ☐ Please charge \_\_\_\_\_ to Deposit Account No. **50-2586** for the above fee(s).

The Commissioner is authorized to charge any fees required by the filing of these papers, and to credit any overpayment to Deposit Account No. **50-2586**.

Respectfully submitted,  
Perkins Coie LLP

Dated: November 12, 2003

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> Form PTO-1449 (Modified) (Use several sheets if necessary)				<b>COMPLETE IF KNOWN</b>	
				Application Number	10/623,189
				Confirmation Number	
				Filing Date	July 18, 2003
				First Named Inventor	DePaoli, Alex M. <i>et al.</i>
				Group Art Unit	
Examiner Name					
Sheet	3	of	7	Attorney Docket No.	54113.8005.US02

FOREIGN PATENT DOCUMENTS						
		Foreign Patent or Application				
	B28		WO 97/20933			
*	B29		WO 97/38014			
*	B30		WO 97/46585			
*	B31		WO 98/08512			
*	B32		WO 98/28427			
*	B33		WO 00/20872			

OTHER PRIOR ART-NON PATENT LITERATURE DOCUMENTS				
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume issue number(s), publisher, city and/or country where published.		
*	C1	ABATE, N., <i>et al.</i> , "Estimation of Adipose Tissue Mass By Magnetic Resonance Imaging: Validation Against Dissection in Human Cadavers," <i>J. Lipid Res.</i> 1994; 35:1490-6.		
*	C2	AHIMA, R.S., <i>et al.</i> , "Role of Leptin in the Neuroendocrine Response to Fasting," <i>Nature</i> 1996: 382:250-2.		
	C3	ARIOGLU, E., <i>et al.</i> , "Efficacy and Safety of Troglitazone in the Treatment of Lipodystrophy Syndromes," <i>An Intern Med.</i> 2000; 133:263-74.		
	C4	BERASAIN, C., <i>et al.</i> , "Pathological and Virological Findings in Patients With Persistent Hypertransaminasaemia of Unknown Etiology," <i>Gut.</i> 2000:47:429-35.		
	C5	BERG, A.H., <i>et al.</i> , "The Adipocyte-Secreted Protein Acrp30 Enhances Hepatic Insulin Action," <i>Nat Med.</i> 2001; 7:947-53.		
	C6	BOLAN, C., <i>et al.</i> , "Intensive, Long-Term Plasma Exchange Therapy For Severe Hypertriglyceridemia in Acquired Generalized Lipoatrophy," <i>J. Clin Endocrin And Metab</i> (Submitted).		
	C7	BURANT, C.F., <i>et al.</i> , "Troglitazone Action Is Independent of Adipose Tissue," <i>J. Clin Invest.</i> 1997; 100:2900-8.		
	C8	CAMPFIELD, L.A., <i>et al.</i> , "Recombinant Mouse OB Protein: Evidence For A Peripheral Signal Linking Adiposity and Central Neural Networks," <i>Science</i> 1995: 269:546-9.		

EXAMINER	DATE CONSIDERED
*EXAMINER: Initial if reference considered, whether or not criteria is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application(s).	

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Form PTO-1449 (Modified)  
(Use several sheets if necessary)



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Attorney Docket No. 54113.8005.US02

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of

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**FOREIGN PATENT DOCUMENTS**

Examiner Initial	Cite No.	Foreign Patent or Application			Name of Patentee or Applicant of Cited Document	Date of Publication or Filing Date of Cited Document	Pages, Columns, Lines, Where Relevant Figures Appear	T
		Office	NUMBER	Kind Code (if known)				
X	B1		EP 725078					
X	B2		EP 725079					
X	B3		EP 736599					
X	B4		EP 741187					
X	B5		EP 744408					
X	B6		EP 745610					
X	B7		EP 835879					
X	B8		WO 96/05309					
X	B9		WO 96/22308					
X	B10		WO 96/23513					
X	B11		WO 96/23514					
X	B12		WO 96/23515					
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X	B18		WO 96/31526					
X	B19		WO 96/34111					
X	B20		WO 96/34885					
X	B21		WO 96/35787					
X	B22		WO 96/37517					
X	B23		WO 96/40912					
X	B24		WO 97/00886					
X	B25		WO 97/06816					
X	B26		WO 97/16550					
X	B27		WO 97/18833					

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OTHER PRIOR ART-NON PATENT LITERATURE DOCUMENTS				
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	C9	CAO, H., <i>et al.</i> , "Nuclear Lamin A/C R482q Mutation in Canadian Kindreds With Dunnigan-Type Familial Partial Lipodystrophy," <i>Hum Mol Genet.</i> 2000; 9:109-12.		
	C10	COSIDINE, R.V., <i>et al.</i> , "Serum Immunoreactive-Leptin Concentrations in Normal-Weight and Obese Humans," <i>N Engl J Med.</i> 1996; 334:292-5.		
	C11	EBIHARA, K., <i>et al.</i> , "Transgenic Overexpression of Leptin Rescues Insulin Resistance and Diabetes in A Mouse Model of Lipoatrophic Diabetes," <i>Diabetes</i> 2001; 50:1440-8.		
	C12	FAROOQI, I.S., <i>et al.</i> , "Effects of Recombinant Leptin Therapy in A Child With Congenital Leptin Deficiency," <i>N Engl J Med.</i> 1999; 341:879-84.		
	C13	FESKANICH, D., <i>et al.</i> , "Reproducibility and Validity of Food Intake Measurements From A Semiquantitative Food Frequency Questionnaire," <i>J Am Diet Assoc.</i> 1993; 93:790-6.		
	C14	FRUEBIS, J., <i>et al.</i> , "Proteolytic Cleavage Product of 30-Kda Adipocyte Complement-Related Protein Increases Fatty Acid Oxidation in Muscle and Causes Weight Loss in Mice," <i>Proc Natl Acad Sci U S A</i> 2001; 98:2005-L0.		
	C15	GARG, A., <i>et al.</i> , "Adipose Tissue Distribution Pattern in Patients With Familial Partial Lipodystrophy (Dunnigan Variety)," <i>J Clin Endocrinol Metab</i> 1999; 84:170-4.		
	C16	GARG, A., <i>et al.</i> , "Peculiar Distribution of Adipose Tissue in Patients With Congenital Generalized Lipodystrophy," <i>J Clin Endocrinol Metab.</i> 1992; 75:358-61.		
	C17	GARG, A., <i>et al.</i> , "Lipodystrophies," <i>Am J Med.</i> 2000; 108:143-52.		
	C18	GAVRILOVA, O., <i>et al.</i> , "Surgical Implantation of Adipose Tissue Reverses Diabetes in Lipoatrophic Mice," <i>J Clin Invest</i> 2000; 105: 271-8.		
	C19	GOTTO, A.M., Jr., "Triglyceride As A Risk Factor For Coronary Artery Disease," <i>Am J Cardiol</i> 1998; 82: 22Q25Q.		

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	C20	HALAAS, J.L., <i>et al.</i> , "Weight-Reducing Effects of the Plasma Protein Encoded By the Obese Gene," <i>Science</i> 1995; 269:543-6.		
	C21	HARRISON, L.C., <i>et al.</i> , "Correlation Between Insulin Receptor Binding in Isolated Fat Cells and Insulin Sensitivity in Obese Human Subjects," <i>J Clin Invest</i> 1976; 58:1435-41.		
	C22	HEYMSFIELD, S.B., <i>et al.</i> , "Recombinant Leptin For Weight Loss in Obese and Lean Adults: A Randomized, Controlled, Dose-Escalation Trial [See Comments]," <i>Jama</i> 1999; 282:1568-75.		
	C23	"Intensive Blood-Glucose Control With Sulphonylureas Or Insulin Compared With Conventional Treatment and Risk of Complications in Patients With Type 2 Diabetes (UKPDS 33)," <i>UK Prospective Diabetes Study (UKPDS) Group, Lancet</i> 1998; 352:837-53.		
	C24	KREISBERG, R.A., "Diabetic Dyslipidemia," <i>Am J Cardiol</i> 1998; 82:67U-73U		
	C25	LAMBRINOUDAKI, I., <i>et al.</i> , "Body Composition Assessment By Dual-Energy X-Ray Absorptionmetry: Comparison of Prone and Supine Measurements," <i>Metabolism</i> 1998; 47:1379-82.		
	C26	LAWRENCE, R.D., "Lipodystrophy and Hepatomegaly With Diabetes, Lipaemia, and Other Metabolic Disturbances: A Case Throwing New Light On the Action of Insulin," <i>Lancet</i> 1946; 1:724-731 and 773-775.		
	C27	LUYCKX, F.H., <i>et al.</i> , "Non-Alcoholic Steatohepatitis: Association With Obesity and Insulin Resistance, and Influence of Weight Loss," <i>Diabetes Metab</i> 2000; 26:98-106.		
	C28	MAGRE, J., <i>et al.</i> , "Identification of the Gene Altered in Berardinelli-Seip Congenital Lipodystrophy On Chromosome 11q13," <i>Nat Genet</i> 2001; 28:365-70.		
	C29	MANTON, N.D., <i>et al.</i> , "Non-Alcoholic Steatohepatitis in Children and Adolescents," <i>Med J Aust</i> 2000; 173:476-9.		

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	C30	MANTZOROS, C.S., et al., "Editorial: Leptin As A Therapeutic Agent-Trials and Tribulations," <i>J Clin Endocrinol Metab</i> 2000; 85:4000-2.		
	C31	MOITRA, J., et al., "Life Without White Fat: A Transgenic Mouse," <i>Genes Dev</i> 1998; 12: 3168-81.		
	C32	MONTAGUE, C.T., et al., "Congenital Leptin Deficiency Is Associated With Severe Early Onset Obesity in Humans," <i>Nature</i> 1997; 387:903-8.		
	C33	PELLEYMOUNTER, M.A., et al., "Effects of the Obese Gene Product On Body Weight Regulation in ob/ob Mice," <i>Science</i> 1995; 269:540-3.		
	C34	PETERS, A.L., et al., "The New Diagnostic Criteria For Diabetes: The Impact on Management of Diabetes and Macrovascular Risk Factors," <i>Am J Med</i> 1998; 105:15s-19s.		
	C35	REITMAN, M.L., et al., "Lipoatrophy Revisited," <i>Trends Endocrinol Metab.</i> 2000; 11:410-6.		
	C36	SHIMOMURA, I., et al., "Decreased IRS-2 and Increased SREBP-1c Lead To Mixed Insulin Resistance and Sensitivity in Livers of Lipodystrophic and ob/ob Mice," <i>Mol Cel</i> 2000; 6:77-86.		
	C37	SHIMOMURA, I., et al., "Insulin Resistance and Diabetes Mellitus in Transgenic Mice Expressing Nuclear SREBP-1c in Adipose Tissue: Model For Congenital Generalized Lipodystrophy," <i>Genes Dev</i> 1998; 12:3182-94.		
	C38	SHIMOMURA, I., et al., "Leptin Reverses Insulin Resistance and Diabetes Mellitus in Mice With Congenital Lipodystrophy," <i>Nature</i> 1999; 401:73-6.		
	C39	TRYGSTAD, O., et al., "Lipodystrophic Diabetes Treated With Fenfluramine," <i>Int J Obes</i> 1977; 1:287-92.		
	C40	UNGER, R.H., et al., "Regulation of Fatty Acid Homeostasis in Cells: Novel Role of Leptin," <i>Proc Natl Acad Sci U S A</i> 1999; 96:2327-32.		

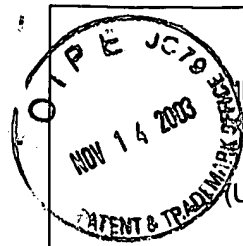
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	C41	UNGER, R.H., <i>et al.</i> , "Lipotoxicity in the Pathogenesis of Obesity-Dependent NIDDM, Genetic and Clinical Implications," <i>Diabetes</i> 1995; 44:863-70.		
	C42	YAMAUCHI, T., <i>et al.</i> , "The Fat-Derived Hormone Adiponectin Reverses Insulin Resistance Associated with Both Lipoatrophy and Obesity," <i>Nat Med.</i> 2001; 7:941-6.		
	C43	ZHANG, Y., <i>et al.</i> , "Positional Cloning of the Mouse Obese Gene and Its Human Homologue," <i>Nature</i> 1994; 372:425-32.		
	C44	ZHANG, Y., <i>et al.</i> , <b>Correction at Nature</b> , 374:479 (1995).		

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		NUMBER	Kind Code (if known)			
	A1	5,521,283				
	A2	5,525,705				
	A3	5,532,336				
	A4	5,552,522				
	A5	5,552,523				
	A6	5,552,524				
	A7	5,554,727				
	A8	5,559,208				
	A9	5,563,243				
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	A14	5,569,743				
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	A19	5,594,104				
	A20	5,605,886				
	A21	5,614,379				
	A22	5,691,309				
	A23	5,719,266				

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[54113-8005-US0200/LA033020.040]